UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office
Address: COMMISSIONER FOR PATENTS
P.O. Box 1450
Alexandria, Virginia 22313-1450
www.uspto.gov

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/845,717	05/02/2001	Soren Nielsen	NIELSEN=3B	3818

7590 03/19/2004

BROWDY AND NEIMARK, P.L.L.C.
624 Ninth Street, N.W.
Washington, DC 20001

EXAMINER	
DEBERRY, REGINA M	

ART UNIT	PAPER NUMBER
1647	

DATE MAILED: 03/19/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/845,717	NIELSEN ET AL.	
	Examiner	Art Unit	
	Regina M. DeBerry	1647	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *18 February 2004*.

2a)☒ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-24* is/are pending in the application.

4a) Of the above claim(s) *3,4,6,7,12-18,21 and 24* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1,2,5,8-10,19,20,22 and 23* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

Status of Application, Amendments and/or Claims

The amendment filed 18 February 2004 has been entered in full. Claim 11 was cancelled. New claims 19-24 were entered.

Applicants state that the restriction requirement is fatally defective in that it does not specify all of the subject matter claimed. Applicants states that Group I relates to the treatment of conditions caused by cancer or a premalignant disorder and Group II to the treatment of conditions caused by infections yet claims 1-5, 8-10, 13 and 16-18 all cover treatment of conditions with other causes. Applicants argue that the restriction as presently phrased, at least nominally denies Applicants to prosecute the opportunity to elect any invention encompassed by claim 1 which is not directed to treatment of cancer or infection. Applicants state that the restriction is also defective in that it fails to address claim 18. Applicants wish to elect with traverse to prosecute at least the invention defined by new claim 20, treatment of inflammation caused by chronic obstructive pulmonary disease (COPD).

Applicants state that the restriction is also traversed because the Examiner has not demonstrated either that Groups I and II are distinct or that it would be a serious burden to search both and that the Examiner has overlooked the point that what is being treated is an inflammatory condition. Applicants state that it should not matter whether that inflammation arises as a result of cancer, infection, or any other causes. Applicants conclude that they do not understand the rationale by which claims 2, 5 and

8-10 are assigned only to Group II and claims 3, 4, 13, 16 and 17 are assigned to only Group I.

Applicants' arguments have been fully considered and are deemed partly persuasive. Because Applicant is free to claim their invention any way they choose, there will be situations wherein restriction within dependent claims are proper. The instant application recites diseases that are not necessarily related. There is no generic feature that links the claims. In addition, non-ischemia conditions, inflammatory conditions and conditions caused by infection are broad terms, which encompass many diseases/conditions. The claims are directed to methods of treating these conditions. While examination may possibly require a search of classes that overlap there is no reason to believe that the search would be co-extensive because a search is directed to references which would render the invention obvious, as well as references directed to anticipation of the invention, and therefore requires a search of relevant literature in many different areas of subject matter. A search of prior art may disclose references, which concern more than one condition, however because the diseases are diverse from one another, a search of all of the conditions in one application would result in undue burden. For example, a method for treating a non-ischemic condition caused by an infection would not necessarily overlap with a method for treating a non-ischemic condition caused by cancer, treating a non-ischemic condition may or may not encompass inflammatory conditions. Furthermore, the instant claims recite the administration of alpha-MSH **and/or** alpha-MSH equivalent **and/or** EPO **and/or** EPO equivalent which would entail a search on different combinations of treatments.

As was stated before, because Applicant is free to claim their invention any way they choose, the Examiner *attempted* to group the claims according to the condition/disease being treated. Certain claims overlapped, thus the Examiner tried to separate out the claims (for examples claims 2/4, 5/13, 8/16, 9/17). Applicants state that they are denied the opportunity to prosecute an election of any invention encompassed by claim 1 which is not directed to treatment of cancer or infection. This is not found persuasive because claims 1 and 3 are so broad that they automatically encompass treatments of conditions that are not drawn to cancer or infection.

Applicants stated that they wish to prosecute the invention of chronic pulmonary obstructive diseases. Therefore, the Examiner will examine claims 1, 2, 5, 8-10, 19, 20, 22 and 23 generically and specifically for a method for treatment or prevention of a non-ischemic condition. The requirement is still deemed proper and is therefore made FINAL. Claims 1, 2, 5, 8-10, 19, 20, 22, 23 are under examination. Claims 3, 4, 6, 7, 12-18, 21 and 24 are withdrawn from further consideration pursuant to 37 CFR 1.142(b), as being drawn to a nonelected Group, there being no allowable generic or linking claim. Applicant timely traversed the restriction (election) requirement 18 February 2004.

The information disclosure statements (filed 02 November 2001, 01 July 2002 and 28 August 2002) were received and comply with the provisions of 37 CFR §§1.97 and 1.98. It has been placed in the application file and the information referred to therein has been considered as to the merits.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 1, 2, 5, 8-10, 19, 20, 22, 23 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the enablement requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

The instant claims are drawn to a method for treatment or prevention of a non-ischemic condition in one or more organ(s) or tissue(s), the method comprising administering of an effective dosage of alpha-MSH and/or of an alpha-MSH equivalent and/or a dosage of EPO and/or an EPO equivalent to the individual in need thereof.

The subject matter sought to be patented as defined by the claims is not supported by an enabling disclosure because the specification does not teach how to prevent a condition/disease. Prevent means to completely stop a condition or disease from occurring. "Prevention" is not a relative term, it is total. The specification is not enabled for a method of preventing or stopping any condition or disease. A very high degree of evidence is required, which is accepted in the art, that an absolute protection from the pathology exists over an extended period of time.

The specification also fails to teach how to make and use alpha-MSH and EPO equivalents and provides no assay to evaluate the function of the equivalent. The specification states that alpha-MSH equivalent is preferably a substance acting on an alpha-MSH receptor and that an EPO equivalent is preferably a substance acting on an EPO receptor. Absent any means to assess the function of the equivalent, it would require an indeterminate quantity of fundamentally unpredictable investigational experimentation of the skilled artisan to determine whether any alpha-MSH or EPO equivalent could be used in the same manner as the native exemplar. Such experimentation would be undue for one skilled in this art.

Furthermore, even were an assay provided, the specification would not support claims to alpha-MSH and EPO equivalents. The term "equivalents" **broadly encompass** sequence variants, mutants, chemicals, analogues, nucleic acid, lipids, macromolecules, etc. In order to make a sequence variant, for example, with the reasonable assurance that it would have the desirable properties of the invention, the artisan would need to know which regions of the disclosed polypeptide are responsible for the interactions underlying its biological function(s). As is well recognized in the art, any modification (even a "conservative" substitution) to a critical structural region of a protein is likely to significantly alter its functional properties. It is known for nucleic acids as well as proteins, that even a single nucleotide or amino acid change or mutation can destroy the function of the biomolecule in many cases. The disclosure provides no guidance as to which regions of the protein would be tolerant of modification and which would not, and it provides no working example of any variant sequence which would be

within the claims. It is in no way predictable that randomly selected mutations, deletions, *etc.* in the disclosed sequence would afford a protein having activity comparable to the one disclosed. Certain positions in the sequence are critical to the protein's structure/function relationship, e.g. such as various sites or regions directly involved in binding, activity and in providing the correct three-dimensional spatial orientation of binding and active sites. These or other regions may also be critical determinants of antigenicity. These regions can tolerate only relatively conservative substitutions or no substitutions (see Wells, 1990, Biochemistry 29:8509-8517).

Lastly, the specification is not enabled for a method of treating or preventing any non-ischemic condition. Non-ischemic conditions can encompass many diverse diseases such as cancer, diabetes, AIDS, hypertension, Alzheimer's disease, osteoporosis, Graves disease, muscular sclerosis, etc. These diseases do not share common pathology. Cancers such as breast, colon and ovarian have very different etiologies. The state of the prior art establishes various treatments for the diseases. Furthermore, the specification is not enabled for a method of treating or preventing chronic obstructive pulmonary disease (COPD). The specification teaches that inflammation of the lungs (asthma) was induced by LPS inhalation (page 26, lines 5-10). LPS inhalation induces a dramatic influx of inflammatory cells in the lung tissue (page 33, lines 25-33). The specification teaches that alpha-MSH, epoitin or the combination of alpha-MSH and epoitin reduced the influx of inflammatory cell in the lung exposed with LPS (page 33, line 35-page 34, line 20). The subject matter sought to be patented as defined by the claims is not supported by an enabling disclosure LPS inhalation is

not an art recognized model for COPD. Shapiro (American Journal of Respiratory Cell and Molecular Biology, 2000) teaches that a variety of chemicals and irritants have been used in experimental animals to induce inflammation and emphysema, including LPS. Shapiro states that all have contributed to the knowledge of lung injury, but none have replicated exposure to cigarette smoke as a model for authentic COPD (page 4, 4th paragraph). Therefore, while alpha-MSH and epoitin appear to reduce the influx of inflammatory cells in the lung tissue after LPS exposure, this is not tantamount to treating COPD.

Due to the large quantity of experimentation necessary to completely stop a non-ischemic condition from occurring, the large quantity of experimentation necessary to make, test and administer alpha-MSH and EPO equivalents compounds in a mammal, the lack of direction/guidance presented in the specification regarding how to make any type of alpha-MSH and EPO equivalents, the absence of working examples directed to same, the complex nature of the invention, and the breadth of the claims which fail to recite limitations regarding structural limitations for alpha-MSH and EPO equivalents, undue experimentation would be required of the skilled artisan to make and/or use the claimed invention in its full scope.

Claims 1, 2, 5, 8-10, 19, 20, 22, 23 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the

inventor(s), at the time the application was filed, had possession of the claimed invention. The specification provides adequate written description for alpha-MSH and EPO but not alpha-MSH and EPO equivalents. The instant claims recite administering alpha-MSH and EPO equivalents.

Vas-Cath Inc. v. Mahurkar, 19USPQ2d 1111, clearly states that "applicant must convey with reasonable clarity to those skilled in the art that, as of the filing date sought, he or she was in possession of the invention. The invention is, for purposes of the 'written description' inquiry, whatever is now claimed." (See page 1117.) The specification does not "clearly allow persons of ordinary skill in the art to recognize that [he or she] invented what is claimed." (See Vas-Cath at page 1116).

With the exception of alpha-MSH and EPO, the skilled artisan cannot envision the detailed chemical structure of the encompassed product, and therefore conception is not achieved until reduction to practice has occurred, regardless of the complexity or simplicity of the method of isolation. The term "equivalents" encompass sequence variants, mutants, chemicals, analogues, nucleic acid, lipids, macromolecules, etc. None of these sequences meet the written description provision of 35 USC 112, first paragraph. Adequate written description requires more than a mere statement that it is part of the invention and reference to a potential method of isolating it. The compound itself is required. See Fiers v. Revel, 25 USPQ2d 1601 at 1606 (CAFC 1993) and Amgen Inc. v. Chugai Pharmaceutical Co. Ltd., 18 USPQ2d 1016.

One cannot describe what one has not conceived. See Fiddes v. Baird, 30 USPQ2d 1481 at 1483. In Fiddes, claims directed to mammalian FGF's were found to

be unpatentable due to lack of written description for that broad class. The specification provided only the bovine sequence.

Therefore, only alpha-MSH and EPO, but not the full breadth of the claim meets the written description provision of 35 U.S.C. §112, first paragraph. Applicant is reminded that Vas-Cath makes clear that the written description provision of 35 U.S.C. §112 is severable from its enablement provision (see page 1115).

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 1,19, 22, 23 are rejected under 35 U.S.C. 102(b) as being anticipated by Delgado Hernandez *et al.*, Neuroimmunomodulation 6:187-192, 1999. The instant claims are drawn to a method for treatment or prevention of a non-ischemic condition in one or more organ(s) or tissue(s), the method comprising administering of an effective dosage of alpha-MSH and/or of an alpha-MSH equivalent and/or a dosage of EPO and/or an EPO equivalent to the individual in need thereof.

Delgado Hernandez *et al.* teach that administration of endotoxin to mice, which induced endotoxemia (non-ischemic condition) and increased circulating TNF alpha and nitric oxide. Delgado Hernandez *et al.* teach that central administration of alpha-MSH

significantly modulated TNF alpha and NO increases in lung and liver. Delgado Hernandez *et al.* teach that lung myeloperoxidase, a marker of neutrophil infiltration was enhanced by LPS injection (induced a non-ischemic condition) and was reduced by administration of alpha-MSH (page 189, results and page 191, 1st and 4th paragraph).

> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 1 and 9 are rejected under 35 U.S.C. 102(b) as being anticipated by Akamatsu *et al.*, US Patent No. 4,745,099. Akamatsu *et al.* teach the administration of human EPO for treatment of the anemia of malignant tumors (non-ischemic condition) (abstract, claims). Akamatsu *et al.* teach the administration of EPO in Lewis lung carcinoma mouse models. Akamatsu *et al.* teach the alleviation of anemia in the carcinoma mouse models upon administration of erythropoietin (column 6, lines 29-52 and Figures 1 and 2).

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Claims 1, 5, 9, 10 are rejected under 35 U.S.C. 103(a) as being unpatentable over Delgado Hernandez *et al.*, Neuroimmunomodulation 6:187-192, 1999 in view of Akamatsu *et al.*, US Patent No. 4,745,099.

The instant claims are drawn to a method for treatment or prevention of a non-ischemic condition in one or more organ(s) or tissue(s), the method comprising administering of an effective dosage of alpha-MSH and/or of an alpha-MSH equivalent and/or a dosage of EPO and/or an EPO equivalent to the individual in need thereof. The teachings of Delgado Hernandez *et al.* are described above. Delgado Hernandez *et al.* do not teach the administration of EPO for a non-ischemic condition.

Akamatsu *et al.* teach the administration of human EPO for treatment of the anemia of malignant tumors (non-ischemic condition) (abstract, claims). Akamatsu *et al.* teach the administration of EPO in Lewis lung carcinoma mouse models. Akamatsu *et al.* teach the alleviation of anemia in the carcinoma mouse models upon administration of erythropoietin (column 6, lines 29-52 and Figures 1 and 2).

It would have been obvious to one of ordinary skill in the art at the time the invention was made to modify the teachings of Delgado Hernandez *et al.* and Akamatsu *et al.* to make the instant invention of a method for treatment of a non-ischemic condition in one or more organ(s) or tissue(s), the method comprising administering of an effective dosage of alpha-MSH and/or of an alpha-MSH equivalent and/or a dosage of EPO and/or an EPO equivalent to the individual in need thereof. The motivation and expected success is provided by both inventors who demonstrate efficacy upon the administration of alpha-MSH or EPO.

Because the instant claims are broadly drawn to "non-ischemic conditions" and both inventors teach the efficacy of treatment of non-ischemic conditions upon administration of alpha-MSH or EPO, it is prima facie obvious to combine two compositions each of which is taught by the prior art to be useful for the same purpose (i.e. treating non-ischemic condition), in order to form a third composition to be used for the very same purpose.... [T]he idea of combining them flows logically from their having been individually taught in the prior art." In re Kerkhoven, 626 F.2d 846, 850, 205 USPQ 1069, 1072 (CCPA 1980) (citations omitted) (Claims to a process of preparing a spray-dried detergent by mixing together two conventional spray-dried detergents were held to be prima facie obvious.). See also In re Crockett, 279 F.2d 274, 126 USPQ 186 (CCPA 1960) (Claims directed to a method and material for treating cast iron using a mixture comprising calcium carbide and magnesium oxide were held unpatentable over prior art disclosures that the aforementioned components individually promote the formation of a nodular structure in cast iron.); and Ex parte Quadranti, 25 USPQ2d 1071 (Bd. Pat. App. & Inter. 1992) (mixture of two known herbicides held prima facie obvious).

Conclusion

No claims are allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Regina M. DeBerry whose telephone number is (571) 272-0882. The examiner can normally be reached on 9:00 a.m.-6:00 p.m.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Gary Kunz can be reached on (571) 272-0887. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

RMD
3/10/04

YVONNE EYLER, PH.D
SUPERVISORY PATENT EXAMINER
TECHNOLOGY CENTER 1600